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Opinion Article

Suspected and Real Problems of Acute Pneumonia

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Opinion:

Abstract:
The principles of providing care to patients with acute pneumonia (AP) that have developed over many centuries were formed exclusively on the basis of empirical experience and were focused on achieving a quick and tangible effect, but, above all, on the basis of subjective assessments. The insufficient development of medical science and the lack of research resources did not allow doctors of that period to purposefully determine the therapeutic potential of the methods used, determine their expediency and place in the treatment of this category of patients.

In the middle of the last century, the situation in this area of medicine began to change rapidly due to the sudden appearance of antibiotics and their first triumph. Antimicrobials, having demonstrated unprecedented success, have been enthusiastically adopted as a universal remedy for many inflammatory diseases. To many specialists, the effect of these drugs seemed truly miraculous, although the danger of their side effects was proven and declared even before the widespread clinical use of this therapy [1-3]. Confidence and optimism regarding the constancy of the effect of this therapy was clearly misleading, since the implementation of the above predictions regarding the development of microflora resistance and a decrease in the activity of antibiotics soon began to be observed.

The main effect of antibiotics is to selectively act only on individual pathogens of inflammatory processes, without affecting the mechanisms of inflammation itself, was known at the beginning of their clinical use. But the desire to maintain initial successes using only one drug has already taken over professional thinking. The narrow etiotropic effect of antibiotics created the illusion of the universality of this therapy and became the main characteristic and the main guideline for further persistent efforts to preserve it. The reason for the improvement in the quality of these drugs was not only the development of resistance of AP pathogens to antimicrobial therapy, but also the resulting changes in the microbial spectrum in the etiology of the disease. To suppress many pathogens that were previously rare in the etiology of AP and suddenly began to increase their presence, new forms of antibiotics were required. This goal and the lack of other ideas for achieving rapid results in helping patients with AP served as an impetus for the development of new antibiotic options, the release of which was most intensively observed in the first decades [4].

The side effects of widespread use of antibiotics increased gradually, but inevitably, having a certain sequence, reflecting the depth and sustainability of the changes occurring. If in the first years of clinical use of antibiotics the emergence and growth of predicted microbial resistance was observed

a parallel decrease in the effectiveness of the first drugs [1-3], then soon it was possible to state a change in the list of pathogens of AP, which was previously stable in the foreseeable period of the pre-antibiotic era [5]. Against the backdrop of such transformations, which are becoming more and more obvious every year, it is puzzling that the role and place of antibiotics in the complex treatment of patients with AP not only have not been subjected to a comprehensive analysis and balanced reassessment, but, despite the radical transformations of the initial conditions, continue to determine a strategy for solving the problem.

The centuries-old history of the development of human society knows many examples when misunderstandings or mistakes, not corrected in a timely manner, served as an erroneous choice of further direction and gave rise to the continuation of a chain of new misconceptions. In the situation we are considering, an important role, undoubtedly, was played by such a circumstance as the prompt introduction of emotional impressions about the first results of the use of antibiotics into medical personnel training programs. The description of preferences and therapeutic value of a new therapeutic direction could only be based on its antimicrobial action. At the same time, no one expressed bewilderment or concern that drugs suddenly appeared that began to act as the main means of treating many (?!) diseases. The fundamental differences between such diseases, on the basis of which a clinical diagnosis was reasonably established and which reflected the unique pathogenesis of each of them, have ceased to play a decisive role in understanding the dynamics and severity of the process. The main cause of inflammatory processes requiring immediate neutralization began to be considered the pathogen and the combination of its aggressive qualities.

This trend in understanding the essence of AP quickly turned into the dominant concept of the disease, which is easy to see by taking another look at the description of this problem and the principles of treating such patients in sections of leading manuals and reference books published in different periods of the era of antibiotics. The main place in such speeches is occupied by a description of the harmful properties of the most active pathogens of AP and a detailed list of antibiotics recommended to suppress them. At the same time, attention is drawn to such a fact as periodic adjustment of such lists in connection with current changes in pathogens and new recommendations for the use of antimicrobial agents. It is also worth noting that the statement of such changes is usually not accompanied by scientific reasoning about the reasons for their occurrence and avoids explanations regarding the emergence of a tendency to change the causative agents of AP after the start of antimicrobial therapy.

A gradual, but increasingly unshakable focus on the causative agent of AP as the main cause of the disease became stronger and consolidated every year due to its presentation in educational programs for the training of medical personnel, as well as the consolidation of this concept in regulations and rules. In this regard, the conditions in which the formation of modern professional views on the problem under discussion took place, and the scope of the doctor's responsibilities in their practical implementation, make it possible to understand the reasons for the prevailing misconceptions. Many years of attempts at early bacteriological diagnosis of AP in order to optimize antimicrobial therapy have not been successful. Attempts to differentially diagnose this disease depending on the strains of bacteria were unsuccessful. Finally, attempts to separate patients with bacterial and viral forms of lung disease into two separate groups were also unsuccessful [6-8]. At the same time, despite the etiological dynamics and polygamy of AP, its clinical manifestations continue to maintain a relatively standard picture, regardless of the type of pathogen. Such circumstances indicate a long-overdue need to pay serious attention to the functional uniqueness of the lungs and the characteristics of the corresponding disorders.

Current events and the observation of new facts that contradict modern aspirations in solving the problem of AP indicate that the results of many years of attempts to achieve success through the rapid recognition of bacterial pathogens of AP and the targeted use of antibiotics have not been analyzed in detail, and the deeper meaning of their negative nature remains misunderstood . Currently, one can observe a continuation of active efforts to continue the previous trend of attempts at early bacteriological diagnosis of AP with confidence in further successes of antibiotics[9-12]. It is very significant that the examples given were published at the peak of the SARS-CoV-2 pandemic, when bacterial infection and antibiotic treatment faded into the background, giving way to the coronavirus. Moreover, the need is again declared and attempts are being made to study the pathogenesis of AP depending on the qualities of the pathogen [13]. True, the authors of such studies focus on virtual molecular cellular structures, trying to obtain information about the micropathogenesis of the action of pathogens in order to develop pathogen-specific strategies, but at the same time completely ignore the pathogenesis of the disease itself.

The leading role of the pathogen, which arose against the background of long-term use of antibiotics, continues today to have a literally hypnotic effect on the search for professional solutions to the problem of AP. Focusing on only a small part of the larger problem and a kind of obsession with continuing repeated studies with negative results will not achieve the goal until many years of experience with antibiotic therapy and, most importantly, its consequences are subjected to careful analysis and study. For example, the information offered to a wide range of readers that with the help of artificial intelligence a new approach to the creation of antimicrobial drugs has been found, which has almost a million options [14], can only frighten with its possible consequences the reader who really understands the side effects of antimicrobials.

The desire to follow modern ideology in solving the problem of AP forces us to look for ways to increase the effectiveness of drugs to eliminate pathogens. The main cause of the disease continues to be considered a microbiological factor, however, the effect of etiotropic drugs has noticeably decreased in recent years, and the process of releasing their new varieties is experiencing significant difficulties. The reason for this situation is considered to be the resistance of microorganisms and the resulting natural need to develop more effective antimicrobial drugs. This quest in recent years has focused on understanding the cellular and molecular mechanisms of action of pathogens and ways to interfere with these

processes for therapeutic purposes. In this regard, I would like to draw attention to the essence of the intentions that need to be realized when solving such a project.

Growing research into molecular cellular transformations in the body of patients with AP reproduces virtual micro-representations of the dynamics of the disease, but such mechanisms do not have direct landmarks and clinical signs that could help in practice. Practical medicine continues to focus its work on the main indicators of vital functions, with the help of which the condition of patients and the effect of therapy can be monitored. Such indicators, as is known, represent an integral result of the interaction of many micromechanisms invisible to us, but it is the general characteristics that make it possible to observe them in real time, measure and evaluate them in the process of constant monitoring. Therefore, a successful therapeutic effect on one of the micromechanisms of the observed symptom of the disease cannot bring the quick emergency effect that is expected from it. To implement such an urgent task in emergency care for this category of patients, it is necessary to use methods that make it possible to almost instantly influence the holistic cause of the observed symptom, and not the individual links of its pathogenesis. In modern medicine, the role of such methods of treating AP is given to antibiotics, which, in terms of their purpose, even theoretically do not correspond to the solution of this problem, which is increasingly confirmed by modern results [15].

In general, the situation that has developed in this section of medicine indicates that approaches to solving the problem under discussion between researchers on the one hand and practitioners on the other are increasingly moving away from each other, although general ideas about the reasons for the development of AP offer a common goal in finding optimal solutions . In contrast to research into the problem of AP, aimed at finding effective etiotropic drugs and neutralizing the consequences of the interaction of the pathogen at the microstructure level, practical medicine in the most severe cases of the disease is forced, first of all, to monitor the dynamics of the vital functions of the patient's body and provide timely support. In this situation, the existing concept of the disease gives rise to a new chain of misconceptions with far-reaching consequences.

Currently, the assessment of the condition of patients with AP is carried out taking into account the aggression of the pathogen, the consequences of which are considered as the leading cause of the observed functional disorders. This interpretation of the causes of severe AP concentrates all attention on the etiology of the disease, without attaching special importance to the localization of inflammation in this category of patients. This approach to assessing the causes of the severity of the disease and the disorders caused by it ignores fundamental information about the functioning of the cardiovascular system. However, the peculiarity of the localization of inflammation in the area of the pulmonary circulation will, regardless of our choice of priorities, determine the exact opposite mechanism of circulatory disorders, in contrast to all other known nosologies of inflammatory processes. When solving the problem of AP, one cannot ignore the uniqueness of the pulmonary circulation with the inverse ratio of its indicators to the parameters of the systemic blood flow and the ability to autonomously regulate the state of the cardiovascular system in the event of a catastrophe in the pulmonary vessels [16-18]. Believing that the bacterial factor is to blame for all failures in the treatment of AP and the development of complications, modern medicine uses the same diagnostic principles in this category of patients, which for many years have served to determine septic conditions in other inflammatory diseases [19,2].

Such an important function in the body as the state of the circulatory system, the primary disorders of which in patients with AP with the onset of inflammation occur in the pulmonary vessels and, in the case of aggressive development of the process, reflect a tendency to secondary systemic hypotension, is assessed using peripheral arterial pressure indicators [19,20]. Thus, in patients with AP, primary disturbances of general blood flow occur in the vessels of the pulmonary circulation, in which normally blood pressure is approximately 6-8 times lower than in the periphery [17,18]. As soon as the pressure in the pulmonary vessels exceeds the permissible norm, their baroreceptors instantly react, including the so-called unloading reflex [16]. But if the appearance of systemic hypotension in the severe development of AP is a sign of extreme adaptation, and the elimination of the reflex root cause brings a positive effect [15], then in peripheral inflammatory processes such a sign indicates the generalization of the infection with the need to replenish the volume of circulating blood [19,20]. Currently, the diagnosis of septic conditions is carried out using uniform scoring systems based on indicators of several vital parameters [19,20]. At the same time, such a characteristic and important test for determining sepsis as bacteriological examination is not provided in such primary diagnostic systems. The widespread use of such approaches to the diagnosis of septic complications means, on the one hand, the recognition of a complete failure in early and accurate recognition of the pathogen with the absence of the possibility of targeted antimicrobial therapy. On the other hand, this is explained by the desire to stratify patients to identify a group requiring immediate intensive treatment. This shift in emphasis to additional methods of assistance remains focused on the characteristics of the causative agent of the process, which continues to play a leading role. The inclusion of patients with AP in such a system for diagnosing sepsis and underestimation of the features of the pathogenesis of the disease leads to new misconceptions in understanding the essence of this problem.

For example, one of the leading indicators is the respiratory rate, but if the appearance of shortness of breath in most nosologies of an inflammatory nature, as a rule, reflects signs of impaired general circulation with the reaction of the lungs to them, then in patients with AP, rapid breathing is one of the early and characteristic symptoms of the underlying disease. An early tendency to arterial hypotension with severe development of pneumonia serves, according to the principles of such scoring diagnostics, as another convincing argument in favor of sepsis. Therefore, extrapolation of such estimates to the condition of patients with severe forms of AP ends with the diagnosis of pseudosepsis. It is no coincidence that the bulk of septic complications, usually exceeding half of all observations, occur in patients with AP [21-25]. The peculiar pathogenesis of general circulatory disorders in this category of patients is indeed accompanied by the development of signs that

correspond to modern ideas about shock. Septic shock, which remains a possible complication in patients with AP, is in fact extremely rare in them, and those general circulatory disorders that are currently classified as sepsis and septic shock are of pulmonary rather than septic origin. This has been confirmed using objective tests rather than analogies and comparisons, and was described approximately 40 years ago [15].

The summary information presented above only about some facts of the essence of modern approaches to solving the problem of AP allows us to note the undoubted and profound influence of antibiotics on the formation of professional ideas about the real sources and mechanisms of this disease. Even today, when many aspects of the exacerbation of the problem of AP with the use of antibiotics have become quite obvious and continue to be confirmed by the accumulation of new facts, a detailed and balanced analysis of the consequences of such therapy remains an unrealized task. The only side effect of antibiotics that has been recognized and steadily increased throughout the period of their use and which has recently suddenly become a global disaster is microbial resistance, but this sudden turn of events has its own explanation.

The dependence of decisions and actions only on the importance of one selected factor led to further natural consequences. The increase in the number of viral forms of AP in recent decades has only caused concern among specialists, but the concept of the disease and the resulting principles of treatment approaches have remained the same. A clear demonstration of such unshakable misconceptions was the events of the SARS-CoV-2 pandemic. Without paying due attention throughout the entire period of antibiotic use to constant changes in the set of main pathogens of AP, without attaching much importance to the gradual shift of etiology towards viruses and without trying to revise the narrow approach to solving the problem, modern medicine unexpectedly received a large influx of patients with coronavirus pneumonia. And although an analysis of the facts of the last two decades raises serious doubts about the suddenness of this catastrophe, medicine was not prepared for such a development of events. To treat coronavirus inflammation of the lung tissue, antibiotics continued to be widely used [26-28], which in such patients lost their purpose. At the same time, a search for the causes of the pandemic was carried out, during which a detailed analysis of the processes occurring over many decades under the influence of antimicrobial drugs gave way to so-called conspiracy theories with the participation of even intelligence services in this work [29].

The first experience of the clinical use of antibiotics clearly showed that their antimicrobial effect is sufficient for the patient's body to quickly cope with the problem that has arisen. This action, which has a literal impact only on the etiology of the disease, was adopted under the impression of the first results as the main thesis for further actions, and the causative agent of the process began to be considered as the main cause of the disease. However, interest was lost in the pathogenesis of the process, to which the new therapy was not directly related. The decrease in the effectiveness of antibiotics due to increased microflora resistance occurred gradually, so the main attention was paid to maintaining the activity of etiotropic therapy, which for a long time was possible to a certain extent due to the release of new drugs. This trend gradually became the main concept of AP, which continues to dominate modern medicine and directs the main efforts in these patients to identifying the pathogen and its suppression.

It is now known that the continuation of previous therapeutic clichés during a pandemic and the search for evidence of the deliberate spread of coronavirus did not bring the desired results, which, from my point of view, is a completely natural consequence of the wrong goals and direction. However, the situation observed during the pandemic required, on the one hand, the mitigation and explanation of medical failures, and on the other, a reduction in the level of anxiety and tension that was growing in society. After years of recognizing the widespread prevalence of resistant microflora and highlighting this burden in various information reports, the World Health Organization (WHO) suddenly, at the peak of the pandemic, declared this phenomenon a global disaster [30]. Although the contents of this document are not directly related to the coronavirus invasion, many were somewhat satisfied with this message and its explanation. A huge audience, including not only specialists who are accustomed to relying on the use of antibiotics for illness, received official notification about the reasons for the decrease in the effectiveness of the main methods of treating AP and an indirect explanation for the large number of failures.

Unfortunately, this WHO document was at least several decades late in publication. Discussing measures to prevent this burden today may not have the same impact that such a company could achieve in the early stages of the emergence of resistant strains. Concerns about the difficulties that arise in the treatment of patients with such pathogens of inflammatory processes arose not now, but many years ago, but their increase is associated not with the characteristics of resistant microflora, which are increasingly present in the form of symbionts in healthy individuals, but with confusion regarding reducing the usual place of antibiotics in the treatment of AP, which are increasingly losing their purpose. But, if in the first decades the decrease in the effectiveness of this therapy was quickly compensated by the release of new drugs, now we have to make allowances for a significant transformation in the etiology of the disease, when more and more pathogens are not detected or are not included in the scope of action of antimicrobial agents.

The proposed text makes another attempt to draw the attention of specialists to a number of undiscussed or rarely reported features of the problem of AP. All these components of the raised topic are a manifestation of biological laws and patterns, as well as an inevitable consequence of damage to various structures of biological objects. Many of these constituent fragments are convincingly proven and relate to the fundamental principles of medical science. Facts of the surrounding reality constantly add new evidence to the accumulated information, allowing us to more fully and comprehensively present the problem under discussion and justify its most optimal solution. Unfortunately, as the results of the period of antibiotic use show, such therapy brought not only biological side effects, but, above all, had a negative didactic impact on the formation of professional ideas about the essence of the problem of AP. It is this consequence of the use of antibiotics

that is currently the main and most important factor on which the direction of research, its further scenario and results depend.

More than 80 years have passed since the first clinical use of antibiotics, but the principle of treating patients with AP, "antibiotics alone," that arose in the early years has turned into a general concept of the disease, although we are talking about the action of drugs with an extremely narrow antimicrobial effect. The classical mechanisms of development of the inflammatory process, its clinical manifestations and methods of emergency pathogenetic correction have strangely remained unclaimed for many years. The lessons of the recent pandemic remain unlearned, but attempts at early diagnosis of bacterial pathogens, despite many years of negative results and the above-mentioned disconfirming facts, continued during this disaster. Clearly, the psychological and mental barrier of the firmly entrenched disease doctrine remains an obstacle that must be overcome. Without this step, the successful solution of the AP problem will remain only a good intention, and the fight against resistant microflora will continue, paradoxically as it sounds today, with the further development of the causes that gave rise to such strains [14,30,31].

One can only welcome such rare in our time, but fair and apt remarks that many methods of respiratory therapy do not stand the test of time and evidence, but nevertheless continue to stubbornly persist in the form of dogma [32]. It's only a pity that this opinion extended to a large number of different methods of respiratory therapy, considering them individually without reference to a specific disease, and was in the nature of a declaration. In relation to the problem under discussion, a radical change in the concept of AP in accordance with the elimination of the above misconceptions allows us to substantiate the pathogenetic principles of treatment, the implementation of which actually represents the existing complex of care for this category of patients as dogmas based on myths [15].

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